Complete Summary

GUIDELINE TITLE

Guidelines on the diagnosis and management of acute pulmonary embolism.

BIBLIOGRAPHIC SOURCE(S)

Torbicki A, Perrier A, Konstantinides S, Agnelli G, Galiè N, Pruszczyk P, Bengel F, Brady AJ, Ferreira D, Janssens U, Klepetko W, Mayer E, Remy-Jardin M, Bassand JP, Vahanian A, Camm J, De Caterina R, Dean V, Dickstein K, Filippatos G, Funck-Brentano C, Hellemans I, Kristensen SD, McGregor K, Sechtem U, Silber S, Tendera M, Widimsky P, Zamorano JL, Zamorano JL, Andreotti F, Ascherman M, Athanassopoulos G, De Sutter J, Fitzmaurice D, Forster T, Heras M, Jondeau G, Kjeldsen K, Knuuti J, Lang I, Lenzen M, Lopez-Sendon J, Nihoyannopoulos P, Perez Isla L, Schwehr U, Torraca L, Vachiery JL, Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the. Guidelines on the diagnosis and management of acute pulmonary embolism: the Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). Eur Heart J 2008 Sep;29(18):2276-315. [400 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Guidelines on diagnosis and management of acute pulmonary embolism. Task Force on Pulmonary Embolism, European Society of Cardiology . Eur Heart J 2000 Aug;21(16):1301-36.

**** REGULATORY ALERT ****

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse (NGC): This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- December 3, 2008 – Innohep (tinzaparin): The U.S. Food and Drug Administration (FDA) has requested that the labeling for Innohep be revised to better describe overall study results which suggest that, when compared to unfractionated heparin, Innohep increases the risk of death for elderly patients (i.e., 70 years of age and older) with renal insufficiency. Healthcare professionals should consider the use of alternative treatments to Innohep when treating elderly patients over 70 years of age with renal insufficiency and deep vein thrombosis (DVT), pulmonary embolism (PE), or both.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Acute pulmonary embolism (PE)
- Venous thromboembolism (VTE)

GUIDELINE CATEGORY

Diagnosis
Management
Risk Assessment
Treatment

CLINICAL SPECIALTY

Cardiology
Critical Care
Emergency Medicine
Family Practice
Internal Medicine
Obstetrics and Gynecology
Pulmonary Medicine
Radiology
Surgery

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide recommendations for the diagnosis, prognostic evaluation, and therapy of acute pulmonary embolism

TARGET POPULATION

Patients at risk for or presenting with pulmonary embolism, including pregnant women

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Risk Assessment

1. Clinical presentation and evaluation of signs and symptoms
2. Assessment of clinical probability of pulmonary embolism
3. Measurement of plasma D-dimer
4. Compression venous ultrasonography and computed tomographic venography
5. Ventilation-perfusion scintigraphy
6. Single-detector of multidetector computed tomography
7. Pulmonary angiography
8. Echocardiography
9. Prognostic assessment
    - Clinical assessment of hemodynamic status (hypotension, shock)
    - Assessment of right ventricular dysfunction (echocardiographic markers, computed tomography-derived indices, biochemical markers)
    - Assessment of myocardial injury (troponin T or I testing, other biomarkers)

Management/Treatment

1. Haemodynamic and respiratory support
    - Vasopressive drugs
    - Correction of systemic hypotension
    - Dobutamine and dopamine
    - Oxygen
2. Thrombolytic therapy
    - Recombinant tissue plasminogen activator (rtPA)
    - Streptokinase
    - Urokinase
3. Surgical pulmonary embolectomy
4. Percutaneous catheter embolectomy and fragmentation
5. Anticoagulant therapy
    - Unfractionated heparin
    - Low molecular weight heparins
    - Fondaparinux
6. Long-term anticoagulation and secondary prophylaxis
    - Vitamin K antagonists
    - Inferior vena cava (IVC) filters (routine use not recommended)
7. Management of specific problems
    - Diagnosis and treatment of pulmonary embolism in pregnancy
    - Anticoagulation in patients with cancer
    - Thrombolysis and embolectomy of right heart thrombi

- Monitoring of platelet counts in heparin-treated patients and management of heparin-induced thrombocytopenia
- Management of chronic thromboembolic pulmonary hypertension
- Management of non-thrombotic pulmonary embolism

MAJOR OUTCOMES CONSIDERED

Diagnosis

Predictive value of diagnostic tests and assessments

Treatment

- Death rates
- Survival rates
- Recurrent pulmonary embolism rates
- Recurrent venous thromboembolic disease rates
- Recurrent deep vein thrombosis rates

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

A. Data derived from multiple randomized clinical trials[a] or meta-analyses
B. Data derived from a single randomized trial[a] or non-randomized studies
C. Consensus of opinion of the experts and/or small studies, retrospective studies, registries

[a] Or large accuracy or outcome trial(s) in the case of diagnostic tests or strategies

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Experts in the field were selected and undertook a comprehensive review of the published evidence for management and/or prevention of pulmonary embolism. A critical evaluation of diagnostic and therapeutic procedures was performed, including assessment of the risk-benefit ratio. Estimates of expected health outcomes for larger societies were included, where data exists. The level of evidence and the strength of recommendation of particular treatment options were weighed and graded according to predefined scales, as outlined in "Rating Scheme for the Strength of the Evidence" and "Rating Scheme for Strength of the Recommendations."

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Classes of Recommendations

Class I: Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.

Class II: Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.

Class IIa: Weight of evidence/opinion is in favour of usefulness/efficacy.

Class IIb: Usefulness/efficacy is less well established by evidence/opinion.

Class III: Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Once the document was finalized and approved by all the experts involved in the Task Force, it was submitted to outside specialists for review. The document was revised and finally approved by the Committee for Practice Guidelines and subsequently published.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the class of recommendations (I, II, IIa, IIb, III) and level of evidence (A, B, C) are provided at the end of the "Major Recommendations."

Note from European Society of Cardiology*: Throughout these guidelines and for the purpose of clinical management, 'confirmed pulmonary embolism (PE)' is understood as a probability of PE high enough to indicate the need for PE-specific treatment and 'excluded PE' as a probability of PE low enough to justify withholding specific PE-treatment with an acceptably low risk despite a clinical suspicion of PE. These terms are not meant to indicate absolute certainty regarding the presence or absence of emboli in the pulmonary arterial bed.*

Diagnosis

Clinical Presentation

Clinical signs, symptoms and routine laboratory tests do not allow the exclusion or confirmation of acute PE but increase the index of its suspicion.

Assessment of Clinical Probability

Clinical evaluation makes it possible to classify patients into probability categories corresponding to an increasing prevalence of PE, whether assessed by implicit clinical judgment or by a validated prediction rule.

D-Dimer

A negative D-dimer result in a highly sensitive assay safely excludes PE in patients with a low or moderate clinical probability, while a moderately sensitive assay excludes PE only in patients with a low clinical probability. When using a recently introduced two-level clinical probability assessment scheme, a negative D-dimer result excludes PE safely in PE-unlikely patients either by a highly sensitive or moderately sensitive assay.

Compression Ultrasonography (CUS) and Computed Tomographic Venography

Searching for a proximal deep vein thrombosis (DVT) in patients with PE by compression venous ultrasonography (CUS) yields a positive result in around 20% of patients. CUS can be used either as a backup procedure to reduce the overall false-negative rate when using single-detector computed tomography (CT) (see "Diagnostic Strategies" below and in the original guideline document) or it can be performed to avoid CT when positive in patients with contraindications to contrast dye and/or irradiation. Combining CT venography with CT angiography adds a significant amount of radiation and is not useful when using multidetector computed tomography (MDCT).

Ventilation-Perfusion Scintigraphy (V/Q Scan)

A normal perfusion scan is very safe for excluding PE. Although less well validated, the combination of a non-diagnostic V/Q scan in a patient with low clinical probability of PE is an acceptable criterion for excluding PE. A high-probability ventilation-perfusion scan establishes the diagnosis of PE with a high degree of probability, but further tests may be considered in selected patients with a low clinical probability due to the lower positive predictive value (PPV) of a high-probability V/Q scan result in such patient. In all other combinations of V/Q scan result and clinical probability, further tests should be performed.

Computed Tomography

A single-detector computed tomography (SDCT) or MDCT showing a thrombus up to the segmental level can be taken as adequate evidence of PE in most instances, whereas the necessity to treat isolated subsegmental thrombi in a patient without a DVT is unclear. In patients with a non-high clinical probability, a negative SDCT must be combined with negative CUS to safely exclude PE, whereas MDCT may be used as a stand-alone test. Whether further testing is mandatory in the rare patients who have a negative MDCT despite a high clinical probability is not settled.

Pulmonary Angiography

Pulmonary angiography is a reliable but invasive test and is currently useful when the results of non-invasive imaging are equivocal. Whenever angiography is performed, direct haemodynamic measurements should be performed.

Echocardiography

In a patient with suspected PE who is in a critical condition, bedside echocardiography is particularly helpful in emergency management decisions. In a patient with shock or hypotension, the absence of echocardiographic signs of right ventricular (RV) overload or dysfunction practically excludes PE as a cause of haemodynamic compromise. The main role of echocardiography in non-high-risk PE is further prognostic stratification to the intermediate low-risk category.

Diagnostic Strategies

Suspected high-risk and non-high-risk PE are two distinct situations that must be distinguished because the diagnostic strategies differ.

It should be recognized that the approach to suspected PE may legitimately vary according to the local availability of tests in specific clinical settings. The most straightforward diagnostic algorithms for suspected PE are presented in Figures 1 and 2 in the original guideline document. In contrast, Table 10 in the original guideline provides the information needed to create alternative evidence-based algorithms whenever necessary.

The recommendations for diagnosis of PE are summarized in the table below.

Recommendations: Diagnosis	Class[a]	Level[b]
Suspected high-risk PE		
• In high-risk PE, as indicated by the presence of shock or hypotension, emergency CT or bedside echocardiography (depending on availability and clinical circumstances) is recommended for diagnostic purposes	**I**	**C**
Suspected non-high-risk PE		
• In non-high-risk PE, basing the diagnostic strategy on clinical probability assessed either implicitly or using a validated prediction rule is recommended	**I**	**A**
• Plasma D-dimer measurement is recommended in emergency department patients to reduce the need for unnecessary imaging and irradiation, preferably using a highly sensitive assay	**I**	**A**
• Lower limb CUS in search of DVT may be considered in selected patients with suspected PE to obviate the need for further imaging tests if the result is positive	**IIb**	**B**
• Systematic use of echocardiography for diagnosis in haemodynamically stable, normotensive patients is not recommended	**III**	**C**
• Pulmonary angiography should be considered when there is discrepancy between clinical evaluation and results of non-invasive imaging tests	**IIa**	**C**
• The use of validated criteria for diagnosing PE is recommended. Validated criteria according to clinical probability of PE (low, intermediate or high) are detailed	**I**	**B**

Recommendations: Diagnosis	Class[a]	Level[b]
below (see also *Table* 10 in the original guideline document)		
Suspected non-high-risk PE		
Low clinical probability		
• Normal D-dimer tenet using either a highly or moderately sensitive assay excludes PE	**I**	**A**
• Normal perfusion lung scintigraphy excludes PE	**I**	**A**
• Non-diagnostic (low or intermediate probability) V/Q scan may exclude PE particularly when combined with negative proximal CUS	**IIa** **I**	**B** **A**
• Negative MDCT safely excludes PE	**I**	**A**
• Negative SDCT only excludes PE when combined with negative proximal CUS	**I**	**A**
• High-probability V/Q scan may confirm PE but... further testing may be considered in selected patients to confirm PE	**IIa** **IIb**	**B** **B**
• CUS showing a proximal DVT confirms PE	**I**	**B**
• If CUS shows only a distal DVT, further testing should be considered to confirm PE	**IIa**	**B**
• SDCT or MDCT showing a segmental or more proximal thrombus confirms PE	**I**	**A**
• Further testing should be considered to confirm PE if SDCT or MDCT shows only subsegmental clots	**IIa**	**B**
Suspected non-high-risk PE		
Intermediate clinical probability		

Recommendations: Diagnosis	Class[a]	Level[b]
• Normal D-dimer level using a highly sensitive assay excludes PE	**I**	**A**
• Further testing should be considered if D-dimer level is normal when using a less sensitive assay	**IIa**	**B**
• Normal perfusion lung scintigraphy excludes PE	**I**	**A**
• In case of a non-diagnostic V/Q scan, further testing is recommended to exclude or confirm PE	**I**	**B**
• Negative MDCT excludes PE	**I**	**A**
• Negative SDCT only excludes PE when combined with negative proximal CUS	**I**	**A**
• High-probability ventilation-perfusion lung scintigraphy confirms PE	**I**	**A**
• CUS showing a proximal DVT confirms PE	**I**	**B**
• If CUS shows only a distal DVT, further testing should be considered	**IIa**	**B**
• SDCT or MDCT showing a segmental or more proximal thrombus confirms PE	**I**	**A**
• Further testing may be considered in case of subsegmental clots to confirm PE	**IIb**	**B**
Suspected non-high-risk PE		
High clinical probability		
• D-dimer measurement is not recommended in high clinical probability patients as a normal result does not safely exclude PE even when using a highly sensitive assay	**III**	**C**

Recommendations: Diagnosis	Class[a]	Level[b]
• In patients with a negative CT, further tests should be considered in selected patients to exclude PE	**IIa**	**B**
• High-probability ventilation-perfusion lung scintigraphy confirms PE	**I**	**A**
• CUS showing a proximal DVT confirms PE	**I**	**B**
• If CUS shows only a distal DVT, further testing should be considered	**IIb**	**B**
• SDCT or MDCT showing a segmental or more proximal thrombus confirms PE	**I**	**A**
• Further testing may be considered where there are subsegmental clots, to confirm PE	**IIb**	**B**

[a] Class of recommendation
[b] Level of evidence

Prognostic Assessment

Clinical Assessment of Haemodynamic Status

Hypotension and Shock

Shock and hypotension are principal markers of high risk of early death in acute PE.

Markers of Right Ventricular Dysfunction (RVD)

RV dysfunction is related to intermediate risk of short-term mortality in acute PE. Prognostic assessment based on signs of RVD is limited by the lack of universally accepted criteria, which in some trials included isolated signs of pulmonary hypertension.

Markers of Myocardial Injury

Myocardial injury in patients with PE can be detected by troponin T or I testing. Positive results are related to an intermediate risk of short-term mortality in acute PE. Prognostic assessment based on signs of myocardial injury is limited by the lack of universally accepted criteria. New markers of injury and the concomitant

assessment of markers of RVD may help improve the substratification of patients with acute PE.

Additional Risk Markers

Multiple variables provided by clinical evaluation and routine laboratory tests are related to the prognosis in acute PE. Consideration of pre-existing patient-related factors may be useful in final risk stratification.

Strategy of Prognostic Assessment

Evaluation of haemodynamic status, signs of RVD and myocardial injury and the assessment of additional patient-related factors are useful for optimal risk stratification.

The recommendations for prognostic assessment of PE are summarized in the table below.

Recommendations: Prognostic Assessment	Class[a]	Level[b]
• Initial risk stratification of suspected and/or confirmed PE based on the presence of shock and hypotension is recommended to distinguish between patients with high and non-high-risk of PE-related early mortality.	**I**	**B**
• In non-high-risk PE patients, further stratification to an intermediate- or low-risk PE subgroup based on the presence of imaging or biochemical markers of RVD and myocardial injury should be considered.	**IIa**	**B**

[a] Class of recommendation
[b] Level of evidence

Treatment

Haemodynamic and Respiratory Support

Haemodynamic and respiratory support is necessary in patients with suspected or confirmed PE presenting with shock or hypotension.

Thrombolysis

Thrombolytic therapy is the first-line treatment in patients with high-risk PE presenting with cardiogenic shock and/or persistent arterial hypotension, with very few absolute contraindications. Routine use of thrombolysis in non-high risk patients is not recommended, but may be considered in selected patients with intermediate-risk PE and after thorough consideration of conditions increasing the

risk of bleeding. Thrombolytic therapy should be not used in patients with low-risk PE.

Surgical Pulmonary Embolectomy

With current surgical techniques pulmonary embolectomy is a valuable therapeutic option in patients with high-risk PE in whom thrombolysis is absolutely contraindicated or has failed.

Percutaneous Catheter Embolectomy and Fragmentation

Catheter embolectomy or fragmentation of proximal pulmonary arterial clots may be considered as an alternative to surgical treatment in high-risk PE patients when thrombolysis is absolutely contraindicated or has failed.

Initial Anticoagulation

Anticoagulation with unfractionated heparin, low-molecular-weight heparin (LMWH) or fondaparinux should be initiated without delay in patients with confirmed PE and those with a high or intermediate clinical probability of PE while the diagnostic workup is still ongoing. Except for patients at high risk of bleeding and those with severe renal dysfunction, subcutaneous LMWH or fondaparinux rather than intravenous unfractionated heparin should be considered for initial treatment.

Therapeutic Strategies

The recommendations for acute treatment of PE are summarized in the table below.

Recommendations: Acute Treatment	Class[a]	Level[b]
High-risk pulmonary embolism		
• Anticoagulation with unfractionated heparin should be initiated without delay in patients with high-risk PE	**I**	**A**
• Systematic hypotension should be corrected to prevent progression of RV failure and death due to PE	**I**	**C**
• Vasopressive drugs are recommended for hypotensive patients with PE	**I**	**C**
• Dobutamine and dopamine may be used in patients with PE, low cardiac output and normal blood pressure	**IIa**	**B**

Recommendations: Acute Treatment	Class[a]	Level[b]
• Aggressive fluid challenge is not recommended	**III**	**B**
• Oxygen should be administered in patients with hypoxaemia	**I**	**C**
• Thrombolytic therapy should be used in patients with high-risk PE presenting with cardiogenic shock and/or persistent arterial hypotension	**I**	**A**
• Surgical pulmonary embolectomy is a recommended therapeutic alternative in patients with high-risk PE in whom thrombolysis is absolutely contraindicated or has failed	**I**	**C**
• Catheter embolectomy or fragmentation of proximal pulmonary arterial clots may be considered as an alternative to surgical treatment in high-risk patients when thrombolysis is absolutely contraindicated or has failed	**IIb**	**C**
Non-high-risk pulmonary embolism		
• Anticoagulation should be initiated without delay in patients with high or intermediate clinical probability of PE while diagnostic workup is still ongoing	**I**	**C**
• Use of LMWH or fondaparinux is the recommended form of initial treatment for most patients with non-high-risk PE	**I**	**A**
• In patients at high risk of bleeding and in those with severe renal dysfunction, unfractionated heparin with an activated partial thromboplastin time (aPTT) target range of 1.52.5 times normal is a recommended form of initial treatment	**I**	**C**
• Initial treatment with unfractionated heparin, LMWH or fondaparinux should be continued for at least 5 days and may be replaced by vitamin K antagonists only after achieving target international normalized ratio (INR) levels for at least 2 consecutive days	**I** **I**	**A** **C**
• Routine use of thrombolysis in non-high-risk PE patients is not recommended, but it may be considered in selected	**IIb**	**B**

Recommendations: Acute Treatment	Class[a]	Level[b]
patients with intermediate-risk PE		
• Thrombolytic therapy should be not used in patients with low-risk PE	**III**	**B**

[a] Class of recommendation
[b] Level of evidence

Long-Term Anticoagulation and Secondary Prophylaxis

Recommendations for long-term anticoagulation are provided in the table below.

Recommendations : Long-Term Treatment	Class[a]	Level[b]
• For patients with PE secondary to a transient (reversible) risk factor, treatment with a vitamin K antagonist (VKA) is recommended for 3 months	**I**	**A**
• For patients with unprovoked PE, treatment with a VKA is recommended for at least 3 months	**I**	**A**
• Patients with a first episode of unprovoked PE and low risk of bleeding, and in whom stable anticoagulation can be achieved, may be considered for long-term oral anticoagulation	**IIb**	**B**
• For patients with a second episode of unprovoked PE, long-term treatment is recommended	**I**	**A**
• In patients who receive long-term anticoagulant treatment, the risk/benefit ratio of continuing such treatment should be reassessed at regular intervals	**I**	**C**
• For patients with PE and cancer, LMWH should be considered for the first 3-6 months... after this period, anticoagulant therapy with VKA or LMWH should be continued indefinitely or until the cancer is considered cured	**IIa** **I**	**B** **C**
• In patients with PE, the dose of VKA should be adjusted to	**I**	**A**

Recommendations : Long-Term Treatment	Class[a]	Level[b]
maintain a target INR of 2.5 (range 2.0-3.0) regardless of treatment duration		

[a] Class of recommendation
[b] Level of evidence

Venous Filters

Recommendations: Venous Filters	Class[a]	Level[b]
• Inferior vena cava (IVC) filters may be used when there are absolute contraindications to anticoagulation and a high risk of venous thromboembolism (VTE) recurrence	**IIb**	**B**
• The routine use of IVC filters in patients with PE is not recommended	**III**	**B**

[a] Class of recommendation
[b] Level of evidence

Specific Problems

Pregnancy

In pregnant women with a clinical suspicion of PE an accurate diagnosis is necessary, because a prolonged course of heparin is required. All diagnostic modalities, including CT scanning, may be used without significant risk to the fetus. Low molecular weight heparins are recommended in confirmed PE; VKAs are not recommended during the first and third trimester and may be considered with caution in the second trimester of pregnancy.

Anticoagulant treatment should be administered for at least 3 months after delivery.

Malignancy

Malignancy is a major predisposing factor for the development and recurrence of VTE. However, routine extensive screening for cancer in patients with a first episode of non-provoked PE is not recommended. In cancer patients with confirmed PE, LMWH should be considered for the first 3-6 months of treatment and anticoagulant treatment should be continued indefinitely or until definitive cure of the cancer.

Right Heart Thrombi

Right heart thrombi, particularly when mobile (i.e., in transit from the systemic veins) are associated with a significantly increased risk of early mortality in patients with acute PE. Immediate therapy is necessary, but optimal treatment is controversial in the absence of controlled trials. Thrombolysis and embolectomy are probably both effective whereas anticoagulation alone appears less effective.

Heparin-Induced Thrombocytopenia (HIT)

HIT is a life-threatening immunological complication of heparin therapy. Monitoring of platelet counts in patients treated with heparin is important for the early detection of HIT. Treatment consists of discontinuation of heparin and alternative anticoagulant treatment, if still required.

Chronic Thromboembolic Pulmonary Hypertension

Chronic thromboembolic pulmonary hypertension (CTEPH) is a severe though rare consequence of PE. Pulmonary endarterectomy provides excellent results and should be considered as first-line treatment whenever possible. Drugs targeting the pulmonary circulation in patients in whom surgery is not feasible or has failed are currently being tested in clinical trials.

Non-thrombotic Pulmonary Embolism

Non-thrombotic PE does not represent a distinct clinical syndrome. It may be due to a variety of embolic materials and result in a wide spectrum of clinical presentations, making the diagnosis difficult. With the exception of severe air and fat embolism, the haemodynamic consequences of non-thrombotic emboli are usually mild. Treatment is mostly supportive but may differ according to the type of embolic material and clinical severity.

Definitions:

Classes of Recommendations

Class I: Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.

Class II: Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.

> **Class IIa**: Weight of evidence/opinion is in favour of usefulness/efficacy.
>
> **Class IIb**: Usefulness/efficacy is less well established by evidence/opinion.

Class III: Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.

Levels of Evidence

Level of evidence A: Data derived from multiple randomized clinical trials[a] or meta-analysis.

Level of evidence B: Data derived from a single randomized clinical trial[a] or large non-randomized studies.

Level of evidence C: Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

[a] Or large accuracy or outcome trial(s) in the case of diagnostic tests or strategies.

CLINICAL ALGORITHM(S)

The following clinical algorithms are provided in the original guideline document:

- Proposed diagnostic algorithm for patients with suspected high-risk pulmonary embolism (PE), (i.e., with shock or hypotension)
- Proposed diagnostic algorithm for patients with suspected non-high-risk PE, (i.e., without shock or hypotension)

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is stated for key recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Improved diagnosis and management of pulmonary embolism, which is a relatively common cardiovascular emergency. Pulmonary embolism is a difficult diagnosis that may be missed because of non-specific clinical presentation. Early diagnosis is fundamental, since immediate treatment is highly effective.

Subgroups Most Likely to Benefit

Primary and secondary risk factors for venous thromboembolism are summarized in Table 3 of the original guideline document.

POTENTIAL HARMS

Pulmonary Angiography

Pulmonary angiography is invasive and not devoid of hazards, including death in rare cases.

Thrombolytic Therapy

Thrombolytic therapy carries a significant risk of bleeding, especially when predisposing conditions or comorbidities exist. Summarized data from randomized trials reveal a 13% cumulative rate of major bleeding and a 1.8% rate of intracranial/fatal hemorrhage.

Percutaneous Procedures

Complications of percutaneous procedures include local damage to the puncture site, usually the femoral vein, perforation of cardiac structures, tamponade, and contrast reactions.

Anticoagulant Therapy

- The most common complication of oral anticoagulant therapy is bleeding.
- Heparin-induced thrombocytopenia is a life-threatening complication of heparin therapy.

Venous Filters

Early complications of permanent inferior vena cava filters, including insertion site thrombosis, occur in 10% of patients. Late complications include recurrent deep vein thrombosis in approximately 20% and the post-thrombotic syndrome in 40% of patients. Occlusion of the vena cava affects approximately 22% of patients at 5 years and 33% at 9 years, regardless of the use and duration of anticoagulation.

Diagnosis and Treatment of Pulmonary Embolism in Pregnancy

- Radiation is absorbed by the fetus during diagnostic tests.
- Warfarin may be associated with central nervous system anomalies in any trimester in pregnancy.
- The overall incidence of bleeding with thrombolytic agents is about 8% (usually from the genital tract and often severe.)

CONTRAINDICATIONS

CONTRAINDICATIONS

Relative contraindications to computed tomography are renal failure and allergy to contrast dye.

Fondaparinux is contraindicated in severe renal failure and with creatinine clearance <20 mL/min.

Isolated oral anticoagulation is contraindicated in the acute phase of heparin-induced thrombocytopenia.

Contraindications to Fibrinolytic Therapy

Absolute Contraindications[a]

- Haemorrhagic stroke or stroke of unknown origin at any time
- Ischaemic stroke in preceding 6 months
- Central nervous system damage or neoplasms
- Recent major trauma/surgery/head injury (within preceding 3 weeks)
- Gastrointestinal bleeding within the last month
- Known bleeding

Relative Contraindications

- Transient ischaemic attack in preceding 6 months
- Oral anticoagulant therapy
- Pregnancy or within 1 week post partum
- Non-compressible punctures
- Traumatic resuscitation
- Refractory hypertension (systolic blood pressure >180 mmHg)
- Advanced liver disease
- Infective endocarditis
- Active peptic ulcer

[a]Contraindications to thrombolysis that are considered absolute, e.g., in acute myocardial infarction, might become relative in a patient with immediately life-threatening high-risk pulmonary embolism.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The European Society of Cardiology (ESC) Guidelines represent the view of the ESC and were arrived at after careful consideration of the available evidence at the time they were written. Health professionals are encouraged to take them fully into account when exercising their clinical judgment. The guidelines do not, however, override the individual responsibility of health professionals to make appropriate decisions in the circumstance of the individual patients, in consultation with that patient, and where appropriate and necessary the patient's guardian or carer. It is also the health professional's responsibility to verify the rules and regulations applicable to drugs and devices at the time of prescription.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm
Personal Digital Assistant (PDA) Downloads
Pocket Guide/Reference Cards
Resources
Slide Presentation
Staff Training/Competency Material

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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GUIDELINE AVAILABILITY

Electronic copies: Available from the European Society of Cardiology (ESC) Web site.

Print copies: Available from Oxford University Press, Great Clarendon Street, Oxford, OX2 6DP, UK, Tel: +44 (0) 1865 353263, Fax: +44 (0) 1865 353774, Web site: http://www.eurheartj.oxfordjournals.org/.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Diagnosis and management of acute pulmonary embolism. Slide set. 2008. Available in Portable Document Format (PDF) from the European Society of Cardiology (ESC) Web site.
- Acute pulmonary embolism. Pocket guidelines. Order form available in Portable Document Format (PDF) from the ESC Web site. Also available for PDA download from the ESC Web site.
- Essential messages from the ESC guidelines. Acute PE. 2009. 6 p. Available in Portable Document Format (PDF) from the European Society of Cardiology (ESC) Web site.

Print copies: Available from Oxford University Press, Great Clarendon Street, Oxford, OX2 6DP, UK, Tel: +44 (0) 1865 353263, Fax: +44 (0) 1865 353774, Web site: http://www.eurheartj.oxfordjournals.org/.

Additionally, continuing medical education (CME) credit is available online at the European Society of Cardiology (ESC) Web site.

PATIENT RESOURCES

None available

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